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(88) Date of publication of the international search report:

7 March 2013

(54) Title: TREATING PRIMARY SCLEROSING CHOLANGITIS

(57) Abstract: A method for treating primary sclerosing cholangitis comprises applying peripheral blood from a patient or subject to an apheresis column loaded with a solid support comprising one or more binding reagents capable of specifically binding to a chemokine receptor, optionally the chemokine receptor CCR9, CXCR4, CCR7 or CCR5 immobilized directly or indirectly on the support thus removing one or more chemokine receptor, optionally CCR9, CXCR4, CCR7 and CCR5 expressing cells from the peripheral blood of the patient or subject. Various companion therapeutic methods and useful binding reagents are also described.



INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2012/051353

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K14/52 A61M1/36 B01J20/32 C07K17/02 G01N33/68
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07K A61M B01J G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EP0-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE 10 2005 036505 A1 (ADEXTER GMBH [DE]) 1 June 2006 (2006-06-01) paragraphs [0023], [0024] -----	4, 11, 25-32
Y	WO 2007/133147 A1 (IBD COLUMN THERAPIES INTERNAT [SE]; THOERN MAGNUS [SE]; WINQVIST OLA [] 22 November 2007 (2007-11-22) claims -----	4, 11, 25-32
X	WO 2010/029317 A2 (IBD COLUMN THERAPIES INTERNAT [SE]; WINQVIST OLA [SE]; COTTON GRAHAM [] 18 March 2010 (2010-03-18) cited in the application the whole document -----	9-15
Y	----- -/-	1-15, 25-32

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2012/051353

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/017979 A1 (MACK MATTHIAS [DE] ET AL) 23 January 2003 (2003-01-23) claims 4, 5, 19 -----	4, 11, 25-32
Y	B. EKSTEEN ET AL: "Hepatic Endothelial CCL25 Mediates the Recruitment of CCR9+ Gut-homing Lymphocytes to the Liver in Primary Sclerosing Cholangitis", JOURNAL OF EXPERIMENTAL MEDICINE, vol. 200, no. 11, 6 December 2004 (2004-12-06), pages 1511-1517, XP055037419, ISSN: 0022-1007, DOI: 10.1084/jem.20041035 cited in the application the whole document -----	1-15, 25-32
Y	GRANT ALLISTER J ET AL: "Hepatic expression of secondary lymphoid chemokine (CCL21) promotes the development of portal-associated lymphoid tissue in chronic inflammatory liver disease", AMERICAN JOURNAL OF PATHOLOGY, vol. 160, no. 4, April 2002 (2002-04), pages 1445-1455, XP002683083, ISSN: 0002-9440 cited in the application the whole document -----	1-15, 25-32
Y	WO 2006/126209 A1 (RAPPAPORT FAMILY INST FOR RES [IL]; KARIN NATHAN [IL]; WILDBAUM GIZI []) 30 November 2006 (2006-11-30) page 3, lines 6-9; claim 29 page 4, lines 28-30; example 2 -----	1-15, 25-32
Y	TERADA RYO ET AL: "Stromal cell-derived factor-1 from biliary epithelial cells recruits CXCR4-positive cells: implications for inflammatory liver diseases", LABORATORY INVESTIGATION, NATURE PUBLISHING GROUP, THE UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY, INC, vol. 83, no. 5, 1 May 2003 (2003-05-01), pages 665-672, XP008155843, ISSN: 0023-6837, DOI: DOI:10.1097/01.LAB.0000067498.89585.06 cited in the application the whole document ----- -/--	1-15, 25-32

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2012/051353

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ANDREA T BORCHERS ET AL: "Lymphocyte recruitment and homing to the liver in primary biliary cirrhosis and primary sclerosing cholangitis", SEMINARS IN IMMUNOPATHOLOGY, SPRINGER, BERLIN, DE, vol. 31, no. 3, 17 June 2009 (2009-06-17), pages 309-322, XP019758214, ISSN: 1863-2300, DOI: 10.1007/S00281-009-0167-2 the whole document -----	1-15, 25-32

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2012/051353

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-15, 25-32(all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-15, 25-32(all partially)

A binding reagent capable of specifically binding the CCR9 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating PSC

2. claims: 1-15, 25-32(all partially)

A binding reagent capable of specifically binding the CXCR4 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating PSC

3. claims: 1-15, 25-32(all partially)

A binding reagent capable of specifically binding the CCR7 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating PSC

4. claims: 1-15, 25-32(all partially)

A binding reagent capable of specifically binding the CCR5 chemokine receptor, immobilized on a solid support within an apheresis column, and its use for treating PSC

5. claims: 19-24

Methods of diagnosing PSC or selecting a suitable treatment for the disease comprising determining the levels of CCR9, CXCR4, CCR7 and/or CCR5

6. claims: 33-37

Modified CCL8/MCP-2 chemokine

7. claims: 38-41

Modified CCL5 chemokine

8. claims: 42-45

A truncated CXCL12 chemokine

9. claims: 46-51

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Modified CCL19 chemokine

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2012/051353

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 102005036505 A1	01-06-2006	NONE	
WO 2007133147 A1	22-11-2007	AU 2007250552 A1 CA 2651883 A1 CN 101443041 A EA 200802086 A1 EP 2021025 A1 JP 2009536944 A KR 20090007642 A SG 171684 A1 US 2009192434 A1 WO 2007133147 A1 ZA 200809429 A	22-11-2007 22-11-2007 27-05-2009 30-06-2009 11-02-2009 22-10-2009 19-01-2009 29-06-2011 30-07-2009 22-11-2007 26-08-2009
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